

PATENT COOPERATION TREATY
PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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|--------------------------------------------------------|--------------------------------------------------------------|-------------------------------------------------------------|---------------------------------------------------------------------|
| Applicant's or agent's file reference 634 | FOR FURTHER ACTION | | see Form PCT/ISA/220 as well as, where applicable, item 5 below. |
| International application No. PCT/DK2004/000840 | International filing date (day/month/year) 02/12/2004 | (Earliest) Priority Date (day/month/year) 03/12/2003 | |
| Applicant LEO PHARMA A/S | | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 12 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
 - a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
 - b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. **Certain claims were found unsearchable** (See Box II).
3. **Unity of invention is lacking** (see Box III).
4. With regard to the **title**,
 - the text is approved as submitted by the applicant.
 - the text has been established by this Authority to read as follows:

HYDROXAMIC ACID ESTERS AND PHARMACEUTICAL USE THEREOF
5. With regard to the **abstract**,
 - the text is approved as submitted by the applicant.
 - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. With regard to the **drawings**,
 - a. the figure of the **drawings** to be published with the abstract is Figure No. _____
 - as suggested by the applicant.
 - as selected by this Authority, because the applicant failed to suggest a figure.
 - as selected by this Authority, because this figure better characterizes the invention.
 - b. none of the figures is to be published with the abstract.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C259/10 A61K31/165 C07D213/84 C07D401/12 C07D413/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C A61K C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X D1 | WO 99/01426 A (WARNER-LAMBERT COMPANY; BARRETT, STEPHEN, DOUGLAS; BRIDGES, ALEXANDER,) 14 January 1999 (1999-01-14) cited in the application page 5, line 3 – line 8; claims 1,7,23,24; examples 6,7,10,13-102 ----- WO 02/06213 A (WARNER-LAMBERT COMPANY; BARRETT, STEPHEN, DOUGLAS; BIWERSI, CATHLIN; K) 24 January 2002 (2002-01-24) cited in the application page 88 – page 119; claims 1,28-31,34; examples ----- -/- | 1-44 |
| X D2 | | 1-44 |

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

28 April 2005

Date of mailing of the international search report

22.06.2005

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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| X D3 | US 5 155 110 A (CONNOR ET AL) 13 October 1992 (1992-10-13) cited in the application column 3, line 28; claim 4; examples 4,25 | 1-10, 12-23, 25-31, 34-44 |
| X D4 | KALGUTKAR A S ET AL: "Amide Derivatives of Meclofenamic Acid as Selective Cyclooxygenase-2 Inhibitor" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 12, 2002, pages 521-524, XP002319950 ISSN: 0960-894X page 522, right-hand column, last paragraph - page 523, left-hand column, paragraph 1; table 2; compounds 12,13,14,15 | 1-10, 12-23, 25-31, 34-44 |
| X D5 | EP 1 321 518 A (WARNER-LAMBERT COMPANY LLC) 25 June 2003 (2003-06-25) page 2, paragraph 6 page 4, paragraph 24 | 1-5,7,9, 10, 12-23, 25-31, 33-44 |
| X D6 | WO 03/062189 A (WARNER-LAMBERT COMPANY LLC; BARRETT, STEPHEN, DOUGLAS; KAUFMAN, MICHAEL) 31 July 2003 (2003-07-31) claim 1; examples; table 1 | 1-44 |
| X D7 | WO 00/35436 A (WARNER-LAMBERT COMPANY; DUDLEY, DAVID, THOMAS; FLORY, CRAIG, MASON; SA) 22 June 2000 (2000-06-22) claims 10,13 | 1-44 |
| X D8 | US 6 147 107 A (DENT ET AL) 14 November 2000 (2000-11-14) column 4, line 6 - line 51; claim 1 | 1-44 |
| X D9 | WO 00/41505 A (WARNER-LAMBERT COMPANY; TECLE, HAILE; BARRETT, STEPHEN, DOUGLAS) 20 July 2000 (2000-07-20) page 14 - page 16; claims 4,5; compounds 5,20 | 1-44 |
| X D10 | WO 00/40235 A (WARNER-LAMBERT COMPANY; BRIDGES, ALEXANDER, JAMES; DUDLEY, DAVID, THOM) 13 July 2000 (2000-07-13) page 56; claim 8; examples 6a-77a; table 1 | 1-44 |
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X D11 | WO 03/062191 A (WARNER-LAMBERT COMPANY LLC; BARRETT, STEPHEN, DOUGLAS; KAUFMAN, MICHAEL) 31 July 2003 (2003-07-31) page 9, line 3 - line 5; claim 1; examples; table 1 | 1-44 |
| X D12 | WO 01/68619 A (WARNER-LAMBERT COMPANY; BIWERSI, CATHLIN; TECLE, HAILE; WARMUS, JOSEPH) 20 September 2001 (2001-09-20) claims 6,16; examples 4,6,61 | 1-44 |
| X D13 | WO 02/076496 A (VAN ANDEL INSTITUTE; DUESBERY, NICHOLAS, S; WEBB, CRAIG, P; VANDE WOUD) 3 October 2002 (2002-10-03) <i>MCFR = Van Glomse</i> claim 6 | 1-44 |
| X D14 | WO 02/18319 A (WARNER-LAMBERT COMPANY; CHEN, MICHAEL, HUAI, GU; DAVIS, EDWARD, MARK;) 7 March 2002 (2002-03-07) page 92; claim 1; examples 15,20-22,27 | 1-44 |
| X D15 | DATABASE BEILSTEIN BEILSTEIN CROSSFIRE INSTITUT ZUR FOERDERUNG DER WISSENSCHAFTEN; BRN 2826119 1989, XP002319951 abstract & MAMALIS ET AL: JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL SOCIETY. LETCHWORTH, GB, 1965, pages 6278-6287, ISSN: 0368-1769 | 1-5 |
| X D16 | DATABASE BEILSTEIN BEILSTEIN CROSSFIRE INSTITUT ZUR FOERDERUNG DER WISSENSCHAFTEN; BRN 2186299 1989, XP002319952 abstract & WOLF ET AL: JUSTUS LIEBIGS ANNALEN DER CHEMIE, VERLAG CHEMIE GMBH. WEINHEIM, DE, 1975, pages 1245-1250, ISSN: 0075-4617 | 1-5 |
| X D17 | DATABASE BEILSTEIN BEILSTEIN CROSSFIRE INSTITUT ZUR FOERDERUNG DER WISSENSCHAFTEN; Citation Number 134310 1988, XP002319953 abstract & ALLAIS A ET AL: CHIMIE THERAPEUTIQUE, EDITIONS DIMEO, ARCEUIL, FR, vol. 8, 1973, pages 154-168, ISSN: 0009-4374 | 1-5 |

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| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
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| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X D18 | GB 1 126 672 A (FARBWERKE HOECHST AKTIENGESELLSCHAFT) 11 September 1968 (1968-09-11) examples 1,3,4 ----- | 1-5 |
| X D19 | SCOTT A W ET AL: "SOME HYDROXYLAMINE DERIVATIVES OF ANTHRANILIC ACID" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY, EASTON, US, vol. 7, no. 6, 1942, pages 508-516, XP002313446 ISSN: 0022-3263 page 509, last paragraph -& DATABASE BEILSTEIN BEILSTEIN CROSSFIRE INSTITUT ZUR FOERDERUNG DER CHEMISCHEN WISSENSCHAFTEN; BRN 3461601 1990, XP002319954 abstract ----- | 1-5 |
| X D20 | WO 95/25723 A (AGREVO UK LIMITED; RIORDAN, PETER, DOMINIC; BODDY, IAN, KENNETH; OSBOU) 28 September 1995 (1995-09-28) claim 1; example 8; compounds 41,67,96 ----- | 1-5,7,9 |
| X D21 | WO 03/024222 A (E. I. DU PONT DE NEMOURS AND COMPANY; BERGER, RICHARD, ALAN; FLEXNER,) 27 March 2003 (2003-03-27) page 122; claim 1; table A; compounds 568,569,570,571 ----- | 1-5 |
| A D22 | WO 02/068406 A (AMGEN INC) 6 September 2002 (2002-09-06) the whole document ----- | 1-44 |
| P,X D23 | WO 2004/037853 A (IRM LLC; HE, YUN; ELLIS, DAVID, ARCHER; ANACLERIO, BETH, MARIE; KUHEN,) 6 May 2004 (2004-05-06) examples 8,9; compound 9 ----- | 1-5 |
| P,X D24 | DATABASE WPI Section Ch, Week 200425 Derwent Publications Ltd., London, GB; Class B02, AN 2004-262131 XP002319955 -& JP 2004 075614 A (SANKYO CO LTD) 11 March 2004 (2004-03-11) abstract; examples I-299 ----- | 1-44 |

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| | & EL-KHAMRY A M ET AL: "Synthesis and reactions of some biologically active 2-(2'-thienyl)benzoxazinone and quinazolinone derivatives." DIE PHARMAZIE. MAY 1989, vol. 44, no. 5, May 1989 (1989-05), pages 312-315, ISSN: 0031-7144 | |
| A <i>D25</i> | DATABASE BEILSTEIN BEILSTEIN INSTITUT ZUR FOERDERUNG DER CHEMISCHEN WISSENSCHAFTEN; BRN 5600004 1993, XP002326586 abstract & EL-KHAMRY A M ET AL: "Synthesis and reactions of some biologically active 2-(2'-thienyl)benzoxazinone and quinazolinone derivatives." DIE PHARMAZIE. MAY 1989, vol. 44, no. 5, May 1989 (1989-05), pages 312-315, ISSN: 0031-7144 | 1-44 <i>~014</i> |
| X <i>D26</i> | KOHL H ET AL: "Cyclisierungreaktionen von o-acylamino-benzhydroxamsäure-O-alkylestern" JUSTUS LIEBIGS ANNALEN DER CHEMIE, VERLAG CHEMIE GMBH. WEINHEIM, DE, vol. 766, 1972, pages 106-115, XP002094547 ISSN: 0075-4617 tables 2,3; compounds 1,4 | 1-5 |
| A <i>D27</i> | WO 02/055501 A (AMGEN INC) 18 July 2002 (2002-07-18) claims; examples | 1,6,8, 26-44 |
| X <i>D28</i> | EP 0 711 757 A (F. HOFFMANN-LA ROCHE AG) 15 May 1996 (1996-05-15) claims 1,8; examples | 1,6,8, 26-29 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2004/000840

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1-44

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-5,7,9-44(part)

compound (I) with X and Y = bond

2. claims: 1-5,7,9-44(part)

compound (I) with X and/or Y is not a chemical bond

3. claims: 6,8,26-44(part)

compound (I) with at least one of D, E, F, G is not a carbon atom

4. claims: 1-5,7,9-44(part)

compound (I) with at least one of R2/R3, R3/R4, R4/R5 forms a fused ring

5. claim: 46(part)

compound (II) which is an acid or ester

6. claim: 46(part)

compound (II) which is a nitrile

7. claim: 46(part)

compound (XV)

8. claim: 45

compound (III)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/DK2004/000840

| Patent document cited in search report | | Publication date | | Patent family member(s) | | Publication date |
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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